GUCY2D gene

guanylate cyclase 2D, retinal

Normal Function

The *GUCY2D* gene provides instructions for making a protein that plays an essential role in normal vision. This protein is found in the retina, which is the specialized tissue at the back of the eye that detects light and color. Within the retina, the GUCY2D protein is located in light-detecting cells called photoreceptors. The retina contains two types of photoreceptor cells: rods and cones. Rods are needed for vision in low light, while cones are needed for vision in bright light, including color vision.

The GUCY2D protein is involved in a process called phototransduction. When light enters the eye, it stimulates specialized pigments in photoreceptor cells. This stimulation triggers a series of chemical reactions that produce an electrical signal, which is interpreted by the brain as vision. Once photoreceptors have been stimulated by light, they must return to their resting (or "dark") state before they can be stimulated again. The GUCY2D protein is involved in a chemical reaction that helps return photoreceptors to their dark state after light exposure.

Health Conditions Related to Genetic Changes

cone-rod dystrophy

At least 10 mutations in the *GUCY2D* gene have been identified in people with a vision disorder called cone-rod dystrophy. The problems associated with this condition include a loss of visual sharpness (acuity), an increased sensitivity to light (photophobia), and impaired color vision. These vision problems worsen over time.

The mutations that cause cone-rod dystrophy occur in one of the two copies of the *GUCY2D* gene in each cell. These mutations are responsible for about one-quarter of the cases of a form of the condition called autosomal dominant cone-rod dystrophy. Most of these mutations affect a particular protein building block (amino acid) in the GUCY2D protein, replacing the amino acid arginine at position 838 with one of several other amino acids. These genetic changes impair normal phototransduction, causing the photoreceptor cells to deteriorate over time. The loss of these cells leads to the progressive vision problems characteristic of cone-rod dystrophy.

Leber congenital amaurosis

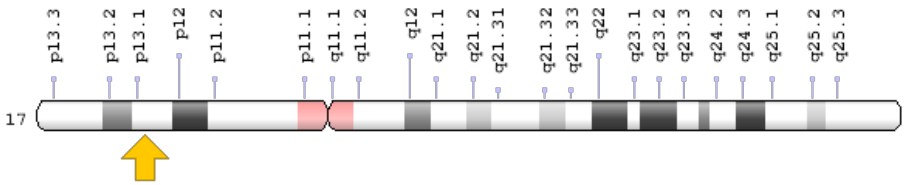
More than 160 mutations in the *GUCY2D* gene have been found to cause Leber congenital amaurosis, a condition characterized by vision loss beginning in infancy. Mutations in this gene account for 6 to 21 percent of all cases of this condition.

The mutations that cause Leber congenital amaurosis occur in both copies of the *GUCY2D* gene in each cell. Most of these genetic changes lead to an abnormally short, nonfunctional version of the GUCY2D protein. A lack of this protein prevents photoreceptor cells from returning to their dark state after they are exposed to light. As a result, the process of phototransduction is almost totally shut down, leading to severe visual impairment beginning very early in life.

Chromosomal Location

Cytogenetic Location: 17p13.1, which is the short (p) arm of chromosome 17 at position 13.1

Molecular Location: base pairs 8,002,670 to 8,020,340 on chromosome 17 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CORD6
- CYGD
- guanylate cyclase 2D, membrane (retina-specific)
- GUC1A4
- GUC2D
- GUC2D_HUMAN
- LCA1
- RCD2
- retGC
- RETGC-1
- RETGC1
- retinal guanylyl cyclase 1
- rod outer segment membrane guanylate cyclase

- ROS-GC
- ROS-GC1
- ROSGC

Additional Information & Resources

Educational Resources

- Neuroscience (second edition, 2001): Functional Specialization of the Rod and Cone Systems
  https://www.ncbi.nlm.nih.gov/books/NBK10850/
- Webvision: The Organization of the Retina and Visual System: Structure of Rods and Cones
  https://www.ncbi.nlm.nih.gov/books/NBK52768/#FuPhototr
  an.2_Structure_of_rods_and_cone

GeneReviews

- Leber Congenital Amaurosis
  https://www.ncbi.nlm.nih.gov/books/NBK1298

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GUCY2D%5BTIAB%5D
  %29+OR+%28RETGC-1%5BTIAB%5D%29+OR+%28RETGC1%5BTIAB%5D
  %29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena
  %5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+
  %22last+3600+days%22%5Bdp%5D

OMIM

- GUANYLATE CYCLASE 2D, MEMBRANE
  http://omim.org/entry/600179

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_GUCY2D.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=GUCY2D%5Bgene%5D
- HGNC Gene Family: Guanylate cyclase receptors
  http://www.genenames.org/cgi-bin/genefamilies/set/343

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4689
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3000
- UniProt
  http://www.uniprot.org/uniprot/Q02846

Sources for This Summary

- Boulanger-Scemama E, El Shamieh S, Démontant V, Condroyer C, Antonio A, Michiels C, Boyard F, Saraiva JP, Letexier M, Souied E, Mohand-Saïd S, Sahel JA, Zeitz C, Audo I. Next-generation sequencing applied to a large French cone and cone-rod dystrophy cohort: mutation spectrum and new genotype-phenotype correlation. Orphanet J Rare Dis. 2015 Jun 24;10:85. doi: 10.1186/s13023-015-0300-3.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26103963
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4566196/
- Hanein S, Perrault I, Olsen P, Lopponen T, Hietala M, Gerber S, Jeanpierre M, Barbet F, Ducroq D, Hakiki S, Munnich A, Rozet JM, Kaplan J. Evidence of a founder effect for the RETGC1 (GUCY2D) 2943DelG mutation in Leber congenital amaurosis pedigrees of Finnish origin. Hum Mutat. 2002 Oct;20(4):322-3.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12325031
- Ito S, Nakamura M, Ohnishi Y, Miyake Y. Autosomal dominant cone-rod dystrophy with R838H and R838C mutations in the GUCY2D gene in Japanese patients. Jpn J Ophthalmol. 2004 May-Jun; 48(3):228-35.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15175914
- Kitiratschky VB, Wilke R, Renner AB, Kellner U, Vadalà M, Birch DG, Wissinger B, Zrenner E, Kohl S. Mutation analysis identifies GUCY2D as the major gene responsible for autosomal dominant progressive cone degeneration. Invest Ophthalmol Vis Sci. 2008 Nov;49(11):5015-23. doi: 10.1167/iovs.08-1901. Epub 2008 May 16.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18487367
- Payne AM, Morris AG, Downes SM, Johnson S, Bird AC, Moore AT, Bhattacharya SS, Hunt DM. Clustering and frequency of mutations in the retinal guanylate cyclase (GUCY2D) gene in patients with dominant cone-rod dystrophies. J Med Genet. 2001 Sep;38(9):611-4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11565546
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1734946/
- Rozet JM, Perrault I, Gerber S, Hanein S, Barbet F, Ducroq D, Souied E, Munnich A, Kaplan J. Complete abolition of the retinal-specific guanylyl cyclase (retGC-1) catalytic ability consistently leads to leber congenital amaurosis (LCA). Invest Ophthalmol Vis Sci. 2001 May;42(6):1190-2.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11328726
- Ugur Iseri SA, Durlu YK, Tolun A. A novel recessive GUCY2D mutation causing cone-rod dystrophy and not Leber's congenital amaurosis. Eur J Hum Genet. 2010 Oct;18(10):1121-6. doi: 10.1038/ejhg.2010.81. Epub 2010 Jun 2.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20517349
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2987461/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/GUCY2D

Reviewed: February 2016
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services